domain wherein said stringent conditions are hybridization in a solution containing 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6-8), 0.1% sodium pyrophosphate, 5x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% sodium dodecyl sulfate (SDS) and 10% dextran sulfate at 42°C followed by wash at 42°C in 0.2 x SSC and 0.1% SDS, which comprises contacting the PSTPIP polypeptide with a candidate antagonist or agonist antibody and monitoring the ability of said polypeptide to induce the polymerization of actin monomers.

Not enough steps

Remarks

The foregoing amendments are fully supported by the specification as originally filed and do not add new matter. Support for the amendments can be found throughout the specification, at least at page 29, lines 27 through 34 and page 13, lines 35 through 38.

It has recently come to Applicants' attention that the filing date on the Official Filing Receipt is incorrect. While the Official Filing Receipt for the current Application indicates a filing date of May 8, 1999, Applicants met the requirements of 35 U.S.C. §371 on May 8, 1998. Thus the date on the Official Filing Receipt appears to be a typographical error. A Request for a Corrected Filing Receipt has been submitted concurrently with this Amendment and a copy has been attached. In anticipation of receiving a corrected filing receipt, the filing date of the present application is presented as May 8, 1998 in the header and in the accompanying declaration and Substitute Sequence Listing.

Oath/Declaration

The Examiner stated that the oath or declaration is defective because it claims the benefit under 35 U.S.C. §120 of an application (serial number 09/938,829) that is entitled differently than the pending application and on which there are no common inventors. Applicants have submitted a new declaration in compliance with 37 CFR 1.67(a) identifying the present application by number and filing date and claiming priority to U.S. application number 08/938,830, filed September 29, 1997, U.S. application number 08/798,419 filed February 7, 1997 and PCT application 98/01774 filed January 30, 1998.

U.S. application number 08/938,830 was originally assigned serial number 08/938,829. However, as two applications had inadvertently been assigned this serial number, the serial

number was later changed to 08/938,830. As the Examiner recognized, the application that now bears serial number 08/938,829 has no relationship to the present application. The new declaration reflects only the change in serial number, and thus Applicants submit that the change is not substantive.

In addition, the Examiner stated that "the oath or declaration claims the benefit of a provisional application, serial number 60/104,589." Applicants have reviewed the declaration that was filed on May 8, 1998 and respectfully submit that no claim to the benefit of a provisional application was made.

Applicants believe that the new declaration is in compliance with 37 CFR 1.67(a) and respectfully request its consideration by the Examiner.

Specification

The Examiner objected to the specification on several grounds. First, the Examiner stated that the specification must be amended to reflect the priority claimed in the declaration. Applicants have amended the specification to reflect the priority claimed in the accompanying new declaration.

Further, the Examiner stated that "this application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b)." Applicants respectfully submit that an abstract on a separate sheet was submitted as page 88 of the application. A replacement sheet has been attached in the event that the Examiner's copy of the application is missing this page. The replacement sheet is a copy of page 88 as originally filed and contains no new matter.

In addition, Applicants have determined that the priority application information in the Substitute Sequence Listing submitted by Applicants on January 6, 2000 contained a typographical error. Applicants intended to claim priority to U.S. Application No. 08/938,830 but inadvertently claimed priority to U.S. Application No. 08/938,300. This has been corrected in the accompanying new sequence listing.

Claim Rejections Under 35 U.S.C. §101

The Examiner rejects claims 15-18 and 22 under 35 U.S.C. §101 "because the claimed invention is not supported by either a specific and substantial asserted utility or a well established

utility." The Examiner discusses the disclosure relating to PSTPIP polypeptides at some length and concludes that a specific and substantial utility is not presented.

Applicants respectfully traverse this rejection and point out that the Examiner's position is in conflict with the recent issuance of U.S. Patent No. 6,111,073, issued on August 29, 2000, on a parent of the present application. The '073 patent claims various PSTPIP polypeptides, including variants encoded by nucleic acid hybridizing under stringent conditions to the complement of the coding sequence of native PSTPIP and retaining certain structural features of the native protein. In the present case, the Examiner states that "the utility of an antibody to a specific protein, such as PSTPIP, is dependent upon the utility of the protein to which it binds." The issuance of a patent with claims covering PSTPIP polypeptides is strong evidence that the Patent Office has acknowledged patentable utility for the protein to which PSTPIP antibodies bind. For the same reason, the antibodies claimed in the present application are believed to have specific utility as required by patent law.

In addition, the Examiner appears to apply an overly strict legal standard by requiring the identification of the exact biological mechanism by which PSTPIP participates in actin polymerization. The Examiner states that "since the specific *biological* function of PSTPIP is not disclosed in the specification or in the art, it is impossible to establish a specific and substantial utility." Thus the Examiner appears to be saying that the exact mechanism through which PSTPIPs participate in a pathway or system must be disclosed in order to establish a utility. The Examiner further establishes this requirement by stating that in the absence of evidence "that PSTPIP is able to induce the polymerization of actin monomers in isolation of other components of the regulatory signaling cascade, one of skill in the art cannot predict that a PSTPIP polypeptide will have the ability to do so."

Applicants strongly disagree and submit that the demonstration of a specific activity is sufficient to demonstrate utility without a demonstration of an exact mechanism. Here, as the Examiner appears to have recognized, PSTPIPs have been shown to play a role in actin polymerization. Thus a specific utility can be based upon this role. For example, antibodies to PSTPIP can be used in vivo to identify rapidly dividing cells, such as those in tumors (page 35, lines 23-24). Similarly, antagonist or agonist antibodies to PSTPIP could be used in vivo to promote or inhibit actin polymerization for therapeutic purposes. These utilities do not require that PSTPIPs stimulate actin polymerization directly or the elucidation of the entire signaling

pathway. The identification of the ability of PSTPIPs to stimulate actin polymerization through a signaling pathway is sufficient to demonstrate their utility to one of skill in the art.

Applicants respectfully submit that even if, as the Examiner appears to contend, each and every biological aspect of the pathway through which the PSTPIPs act has not been exhaustively characterized, a specific and substantial utility can still be asserted, as was recognized by the Patent Office in the issuance of claims to the PSTPIP polypeptides and variants.

The Examiner also contends that "because of sequence differences inherent to a variant or homologue of mouse PSTPIP, one skilled in the art cannot predict, based on sequence homology alone, that said variant or homologue will have the same activity as that protein to which it is being compared...." Again, the Examiner's position is contrary to that taken by the Patent Office in issuing claims to PSTPIP variant polypeptides in U.S. Patent No. 6,111,073. The Examiner cites several references for the idea that changes in amino acid sequence can change the biological function of a protein. Applicants submit that claims 15 and 22 require not only hybridization, but also that the polypeptide encoded by the hybridizing sequence retain the ability to bind to a protein tyrosine phosphatase. Thus the variants will not include those that contain inactivating changes. One skilled in the art will recognize that a variant that retains specific functional attributes will function in substantially the same way as the species that was disclosed, especially in light of the limited amount of sequence variability allowed by the stringent hybridization conditions. Based on the requirements for structural and functional attributes, the variants have a specific and substantial utility.

The Examiner goes on to state that the asserted utilities lack specificity because many unrelated proteins may have similar utilities. For example, the Examiner states that the asserted utility for an antibody that recognizes dividing cells is not specific because "an antibody to any other protein that is expressed in dividing cells could be used in this instance; an antibody to cyclin A, for example, is commonly used to identify cycling cells and could be used to image tumors comprising actively dividing cells." Applicants respectfully submit that the Examiner's position is untenable. It is not the case that simply because one "useful" way of doing a particular thing is already known, any other way is inherently not useful. Under the Examiner's reasoning, once one useful invention is made in a field, no other invention would have a "specific" utility. This is clearly not the case and Applicants submit that as the utilities they have identified are based on the specific biological activity of PSTPIPs, the utilities are specific.

Applicants respectfully submit that substantial and specific utilities have been asserted for PSTPIPs, as recognized by the Patent Office in the issuance of U.S. Patent No. 6,111,073, as well as for antibodies to PSTPIPs, and request that this rejection be withdrawn.

Claim Rejections Under 35 U.S.C. §112

Claims 15 through 18 and 22 were also rejected under 35 U.S.C. §112 first paragraph. The Examiner states that "since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention."

Applicants believe that the Examiner's position cannot be maintained in view of the recent issuance of U.S. Patent No. 6,111,073 for PSTPIP polypeptides and further in view of the foregoing arguments. As discussed above, the present invention is useful. One skilled in the art would know how to use the invention based on the disclosure and, as a result, this rejection should be withdrawn.

Additionally, the Examiner rejects claim 22 "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." The Examiner appears to be suggesting that because PSTPIP polypeptides act in a cascade of signaling events and are not shown to directly catalyze actin polymerization "one cannot use the invention, as claimed, to identify an agonist or antagonist of the ability to induce polymerization of actin monomers."

Applicants respectfully submit that the Examiners' conclusion that it is not possible for one of skill in the art to use the invention as described to identify an antibody agonist or antagonist of PSTPIP is unfounded. The Examiner himself states that "it seems that PSTPIP acts in concert with a number of other proteins to transmit signals that regulate diverse biological activities, including but not limited to actin monomer polymerization...." For the purposes of this rejection, it is irrelevant whether or not the exact physiological mechanisms are understood. One skilled in the art can observe a result of PSTPIP overexpression, actin polymerization, as described in the specification. One skilled in the art can also introduce a candidate antibody to a cell. Finally, one skilled in the art can determine the effect of the candidate antibody on the ability of PSTPIP overexpression to induce actin polymerization. Thus one skilled in the art can

readily determine if the candidate molecule has agonist or antagonistic effects. Applicants submit that this does not depend on the ability of PSTPIP to stimulate actin polymerization in isolation, is sufficiently described in the specification, and thus request that this rejection be withdrawn.

In addition, the Examiner states that "in order to practice the invention as claimed, the integrity of a cell membrane would necessarily have to be disrupted in order to contact PSTPIP with an antibody; and one would not expect PSTPIP to function normally in a disrupted, non-viable cell." Applicants respectfully disagree with the Examiner and submit that a number of methods were known for conferring membrane permeability to otherwise impermeable proteins at the time the application was filed. Several of these methods are described below. A copy of each of the cited references is attached for the Examiner's convenience.

One such method involves the use of protein-transduction domains (PTDs) for the entry of proteins and even larger macromolecular complexes across intact cell membranes. The approach is based on the unique property of certain proteins, such as HIV Tat (Green and Lowenstein, *Cell* 55: 1179-1188 (1988); Frankel and Pabo, *Cell* 55: 1189-1193 (1988); Mann and Frankel, *EMBO J.* 10: 1733-1739 (1991); and Vives, *et al.*, *J. Biol. Chem.* 272: 16010-16017 (1997)), *Drosophila* Antennapedia (Antp) (Derossi, *et al.*, *J. Biol. Chem.* 269: 10444-10450 (1994); and Derossi, *et al.*, *J. Biol. Chem.* 271: 18188-18193 (1996)) and the herpes simplex virus VP22 (Elliott and O'Hare, *Cell* 88: 223-233 (1997)), which contain small, 10 to 16 residue domains that allow these proteins, as well as heterologous proteins attached to them, to cross the intact cell membrane. Although the precise mechanism has not been fully established, the approach has already been used successfully to introduce proteins into cells *in vitro* as well as *in vivo*. For example, Fawell, *et al.* (*Proc. Natl. Acad. Sci. USA* 91: 664-668 (1994)) chemically cross-linked PTD peptides from Tat with β-galactosidase, horseradish peroxidase, RNase A, and *Pseudomonas* exotoxin A, and demonstrated successful delivery of these proteins into a variety of cells *in vitro* as well as *in vivo*. One to two Tat peptides/molecule of protein were sufficient to induce efficient translocation. Theodore, *et al.* (*J. Neurosci.* 15: 7158-7167 (1995)) used the same approach and delivered a highly specific peptide inhibitor of protein kinase C into neural cells, which provoked a change in growth cone morphology, thus suggesting that the delivered peptides retained biological function. In addition, Schutze-Redelmeier, *et al.* (*J. Immunol.* 157: 650-655 (1996)) exploited this approach to deliver antigenic peptides to the MHC class I

processing and presentation pathway *in vitro* and *in vivo*, which led to elicitation of a highly specific CTL response. Some of the potential applications of PTDs derived from Antp have been reviewed by Prochiantz (*Curr. Opin. Neurobiol.* 6: 629-634 (1996)).

Another approach to confer membrane permeability to proteins that would otherwise not enter cells is the use of "membrane transport signals" (MTS). MTS sequences are very hydrophobic peptides derived from secretory signals and are believed to spontaneously partition into the hydrophobic region of membranes. MTS peptides were used to deliver the functional nuclear localization signal (NLS) of the transcription factor NFκB p50 subunit, which resulted in the inhibition of subcellular traffic of NFκB/Rel complexes from the cytoplasm to the nucleus in cultured cells stimulated with pro-inflammatory agonists (Lin, *et al.*, *J. Biol. Chem.* 270: 14255-14258 (1995)). The same approach was used by Rojas, *et al.* (*J. Biol. Chem.* 271: 27456-27461 (1996)) to deliver synthetic phosphopeptides encompassing the autophosphorylation site of epidermal growth factor (EGF) receptor in order to intervene in intracellular signal transduction and gene transcription. Certain other peptides, such as those derived from fusogenic proteins of influenza virus, have also been used to achieve intracellular delivery of proteins and peptides.

Thus various methods for targeting proteins to intracellular locations were known in the art at the time of filing of the instant application. The specification provides sufficient detail to allow one of ordinary skill in the art to determine if a candidate antibody is an antagonist or agonist and Applicants submit that this rejection should be withdrawn.

The Examiner also rejected claims 15-18 and 22 under §112, first paragraph, because the specification "does not reasonably provide enablement for claims drawn to an antibody capable of specific binding to a PSTPIP polypeptide comprising an amino acid sequence encoded by a nucleic acid which hybridizes under specifically claimed stringent conditions to the complement of the nucleic acid molecule comprising the polynucleotide sequence indicated by SEQ ID NO: 2...." The examiner states that "one cannot extrapolate the teachings of the specification to the scope of the claims" because no wash step or conditions for such were recited in the claims. The Examiner also states that while "claims 15 and 22 recite that the antibody is capable of binding a polypeptide encoded by a hybridizing nucleic acid molecule, which 'substantially retains the ability to bind a protein tyrosine phosphatase,'" the meaning of the language 'substantially retaining the ability to bind' cannot be ascertained.

Claims 15 and 22 have been amended to include recitation of a wash step. Support for these amendments can be found at least at page 13, lines 35 through 38. In addition, without acquiescing to the Examiner's position, claims 15 and 22 have been amended to remove the term "substantially." Applicants submit that in view of these amendments, this rejection should be withdrawn.

In addition, the Examiner rejects claims 15-18 and 22 under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has (*sic*) possession of the claimed invention." The Examiner states that "the written description is not commensurate in scope with an antibody capable of binding to a polypeptide encoded by a nucleic acid molecule that hybridizes under specifically claimed stringent conditions to the complement of the polynucleotide indicated by SEQ ID NO: 2."

The Examiner further states that the instant specification fails to provide sufficient descriptive information about "the claimed genus of polynucleotides." Applicants respectfully point out that the claims at issue are not limited to polynucleotides. Claim 15 is directed to antibodies and claim 22 is directed to an assay for identifying agonist or antagonist antibodies. However, as the Examiner has recognized, the claimed antibodies and assay are dependent upon polypeptides that may include those encoded by nucleic acid which hybridizes under stringent conditions to the complement of nucleic acid of SEQ ID NO: 2.

The Examiner states that "the instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera." Applicants submit that a single species of nucleic acid was not disclosed. Rather, both the mouse and human nucleotide sequences were disclosed (SEQ ID NO: 1 and 28) along with the polypeptide sequences (SEQ ID NO: 2 and 29). Thus two species that are within the scope of the genus have been disclosed and reduced to practice.

Further, the Examiner states that "adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required." Applicants respectfully submit that only a representative number of species need be disclosed. Whether a representative number of species is disclosed depends on whether one of skill in the art would recognize that Applicants were in possession of the

necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed or claimed.

The Examiner states that "the instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides." Applicants strongly disagree. The genus is restricted to those polypeptides with specific structural and functional features. In the present case, one skilled in the art will recognize that the stringent hybridization conditions will produce insubstantial variation among the species within the genus. The stringent conditions will yield structurally similar DNAs. In addition, both claim 15 and claim 22 indicate that members of the genus must posses the functional ability to bind to a protein tyrosine phosphatase.

Applicants submit that based on the stringent hybridization requirement and the requirement of functionality, a representative number of species are disclosed and this rejection should be withdrawn.

Finally, claims 15-18 and 22 are rejected under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention." In particular, the Examiner states that the claims are indefinite because they recite the term 'substantially.' As discussed above, without acquiescing to the Examiner's position, Applicants have amended claims 15 and 22 so that they no longer recite 'substantially,' thus obviating this rejection.

Claim Rejections Under 35 U.S.C. §102(b)

Claims 15 and 16 were rejected by the Examiner under 35 U.S.C. §102(b) as being anticipated by Sodhi et al. (*Biochemistry and Molecular Biology International*, 35:559-565 (1995)). Sodhi et al. teach the use of FITC labeled anti-phosphotyrosine antibodies to study tyrosine-phosphorylation of proteins in monocytes/macrophages in response to tumor cells. Anti-phosphotyrosine antibodies specifically recognize phosphorylated tyrosine residues in any polypeptide. They are not specific for PSTPIPs and will only recognize PSTPIPs if they contain a phosphorylated tyrosine residue. Phosphorylation is an important regulatory event and only a fraction of a given population of a protein will be in a phosphorylated state at a given time. Thus in contrast to the antibodies of claim 15, the antibodies taught by Sodhi et al. will not always recognize PSTPIP proteins.

Nevertheless, the Examiner states that "the prior art antibody clearly anticipates the claims since the antibody is known to be capable of specifically binding a polypeptide comprising the amino acid sequence indicated by SEQ ID NO: 1." Without acquiescing to the Examiner's position, Applicants have amended claim 15 to recite "an antibody capable of specific binding to a polypeptide epitope of a PST phosphatase interacting protein...." Thus, in contrast to the antibodies taught by Sodhi et al., the antibodies of claim 15 are not directed to a single amino acid residue or a specific post-translationally modified amino acid residue. Applicants respectfully submit that because the anti-phosphotyrosine antibodies taught by Sodhi et al. recognize only a phosphorylated tyrosine residue and not a polypeptide epitope, they do not anticipate the antibodies of claim 15. As claim 16 depends from claim 15, this rejection should also be withdrawn.

The Examiner rejects claims 15 and 17-18 as being anticipated by Frackleton et al. (*Journal of Biological Chemistry* 259:7909-7915 (1984)). Like Sodhi et al., Frackleton et al. teach the use of an anti-phosphotyrosine antibody. However, the anti-phosphotyrosine antibody taught by Frackleton et al. is a monoclonal antibody. The Examiner states that "In light of the specification, it is clear that an anti-phosphotyrosine monoclonal antibody specifically binds PSTPIP."

As discussed above, anti-phosphotyrosine antibodies are specific for a phosphorylated tyrosine residue and will recognize any protein that contains a phosphorylated tyrosine residue. Because a tyrosine residue is not permanently phosphorylated in PSTPIPs, the antibodies taught by Frackleton et al. will not always bind a PSTPIP protein.

In addition, the antibodies taught by Frackleton et al. are not specific for a polypeptide epitope from a PSTPIP polypeptide. In light of the amendment to claim 15, Applicants respectfully submit that the antibodies taught by Frackleton do not anticipate the antibodies of claim 15 and respectfully request that this rejection be withdrawn. As claims 17 and 18 depend from claim 15, the rejection of these claims should also be withdrawn.

Claims 15 and 17 were also rejected under 35 U.S.C. §102(b) as being anticipated by Su et al. (*Biotechniques* 13:756-762 (1992)). Su et al. describe the use of anti-FLAG antibodies for the immunoaffinity purification of recombinant TNF-α containing FLAG peptide. The Examiner states that "the prior art antibody clearly anticipates the claims since said antibody is known to be

capable of specifically binding a polypeptide comprising the amino acid sequence indicated by SEQ ID NO: 1."

Applicants respectfully submit that anti-FLAG antibodies would not react with PSTPIP polypeptides and clearly do not anticipate the instant claims. Anti-FLAG antibodies are specific to epitopes present on the FLAG polypeptide. As the sequence of the FLAG polypeptide differs from the sequence of the PSTPIPs, the PSTPIPs will not contain epitopes that are recognized by Anti-FLAG antibodies.

It appears to Applicants that the Examiner is saying that anti-FLAG antibodies would bind to a recombinant PSTPIP containing FLAG peptide. However, the present claims are not drawn to such a molecule. The fact that antibodies are known that recognize polypeptides which could be incorporated in a chimeric protein with PSTPIP is irrelevant. The present claims are clearly directed to "an antibody that is capable of specific binding to a polypeptide epitope of a PST phosphatase interacting (PSTPIP) polypeptide." They are not drawn to antibodies that recognize chimeric proteins.

Because the Su et al. reference does not anticipate claims 15 and 17, Applicants respectfully request that this rejection be withdrawn.

The Examiner has also rejected claim 15 as being anticipated by Parthun et al. (Journal of Biological Chemistry 265:209-213 (1990)). Parthun et al. teach the use of an antibody directed against a yeast Gal4 transactivator protein in the analysis of Gal4 activity. The Examiner performed a sequence homology search using PSTPIP nucleotide sequence as a query against the Geneseq database. The Examiner states that the search "revealed that the polynucleotide indicated by SEQ ID NO: 2, which encodes PSTPIP polypeptide comprising SEQ ID NO: 1, is 100% identical over a span of 344 nucleotides to the sequence of a nucleic acid molecule encoding GAL4 transactivating protein." Based on the discovery of this nucleotide homology, the Examiner asserts that "It is clear that the GAL4 gene encodes a protein that is identical in amino acid sequence to at least a portion of the amino acid sequence comprising SEQ ID NO: 1." The Examiner concludes that "The prior art antibody anticipates the claims since said antibody will be capable of specifically binding a polypeptide comprising the amino acid sequence indicated by SEQ ID NO: 1 upon recognition of commonly displayed antigenic epitopes."

Applicants respectfully submit that closer analysis of the aligned nucleotide sequences reveals that the asserted homology resides in a 5'-untranslated region of PSTPIP nucleic acid

(SEQ ID NO: 2). While the coding sequence for PSTPIP polypeptide extends from nucleotide 682 to 1296, the sequence shown in the alignment covers nucleotides 64 to 418. Because the area of homology is in an area that is not translated, the GAL4 gene does not encode a protein that is identical to any part of the amino acid sequence of SEQ ID NO: 1. As a result, the prior art antibody will not be capable of specifically binding to a polypeptide epitope as claimed, and this rejection should be withdrawn.

Claim Rejections Under 35 U.S.C. §103(a)

Claims 15 and 16 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Bennett et al. or Geneseq Data Bank search result 3, in view of U.S. Patent No. 5,001,225-A. The Examiner states that Bennett, et al disclose the sequence of a GAL4 polynucleotide "having 100% identity with the nucleic acid molecule indicated by SEQ ID NO: 2 ... over a range of 344 nucleotides." While Bennett et al. did not expressly disclose an antibody, the Examiner concludes that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention (*sic*) to make a polyclonal antibody to the encoded polypeptide...." Thus the Examiner argues that the GAL4 amino acid sequence would share 100% sequence identity with a part of the PSTPIP polypeptide and, therefore, that anti-GAL4 antibodies would recognize some of the common epitopes on PSTPIP polypeptides. The Examiner also states that it would have been obvious to conjugate the antibody to a detectable label, as taught in U.S. Patent No. 5,001,225-A.

Applicants respectfully point out that Bennett et al. disclose the same sequence as that disclosed in the Parthun et al. reference discussed above. Again, the nucleotide sequence identity between GAL4 and PSTPIP corresponds only to 5'-untranslated PSTPIP sequence. Thus there is no homology at the amino acid level and anti-GAL4 antibodies would not recognize any epitopes on PSTPIP polypeptides. As a result, the antibodies of claims 15 and 16 are not rendered obvious by these references and the Examiner is respectfully requested to withdraw this rejection.

Claim 15 was also rejected under 35 U.S.C. §103(a) as allegedly being obvious over Green Cross Corp. (Geneseq Accession No. Q61607; JO6078767-A, 1994) and Geneseq Data Bank search result 6. The Examiner states that JO6078767-A discloses the sequence of a polynucleotide having 100% sequence identity with the nucleic acid molecule indicated by SEQ

ID NO: 2 ... over a range of 280 nucleotides (see Geneseq Data Bank search result 6)." The Examiner goes on to state that "nucleic acid molecules with identical polynucleotide sequences will encode polypeptides with identical amino acid sequences translated from the same open reading frame."

Applicants respectfully point out that the nucleotide sequence homology lies in the 5'-untranslated region of the PSTPIP nucleotide sequence (SEQ ID NO: 2). The coding sequence for the PSTPIP polypeptide extends from nucleotide 682 to nucleotide 1926 in SEQ ID NO: 2, while the area of identity shown in search result 6 extends from nucleotide 72 to nucleotide 418. As a result, the identified nucleotide identity does not translate into amino acid sequence identity. Therefore, there is no indication that anti-GAL4 antibodies would recognize PSTPIP polypeptides and this rejection should be withdrawn.

Conclusion

For the reasons presented above, Applicants respectfully submit that all pending claims are in condition for allowance, and an early action to that effect is respectfully solicited. If any issues remain or require further clarification, the Examiner is respectfully requested to call Applicants' counsel at the number listed below in order to resolve such issues promptly.

Respectfully submitted,

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Dated: January 23 2001

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